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EXAMINER	
PARKIN, J	
ART UNIT	**PAPER NUMBER**
1813	5

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DATE MAILED: 12/06/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☑ Responsive to communication filed on 09/15/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 42-61 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 42-61 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☒ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Detailed Office Action

15. Acknowledgement is hereby made of Paper Nos. 2 and 3 containing preliminary amendments A and B, which include a response to the notice to file missing parts. Applicants have correctly noted that continuing applications with a domestic priority date preceding the sequence rule implementation date (October 1, 1990) are not required to comply with 37 C.F.R. § 1.821-1.825 as set forth under M.P.E.P. § 2421.08. In the instant application claims 1-41 have been canceled without prejudice or disclaimer while claims 42-61 are currently pending.

16. Acknowledgement is hereby made of applicants' claim for domestic priority under 35 U.S.C. § 120 based upon a series of applications dating to Serial No. 06/835,228, filed March 03, 1986. Perusal of these applications demonstrates that the claimed methods and HIV-2_{ROD} nucleic acids corresponding to the LTR (U3-R region) and regions capable of encoding the disclosed *gag* and *env* products receive support in application Serial No. 07/003,764, filed January 16, 1987. Accordingly, claims 42-61 will receive an effective priority date of January 16, 1987.

Applicants have also requested foreign priority under 35 U.S.C. § 119 corresponding to a series of foreign applications dating to January 22, 1986. Certified copies of the appropriate foreign priority documents were presumably placed in a prior related application. However, at the time of this office action these documents were not available for review. Submission of these documents would facilitate the evaluation of the applicants' claim to foreign priority.

17. The drawings filed in this application are objected to by the Draftsperson under 37 C.F.R. 1.84 or 1.152 as indicated. These informal drawings are acceptable for examination purposes only. Formal drawings with the appropriate corrections will be required when the application is allowed.

18. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention (i.e. failing to provide an enabling disclosure). Claims 42-51 are directed towards methods for the detection of HIV-2 RNA employing nucleic acid probes derived from the HIV-2 LTR, *gag*, and *env* regions of the genome. Claims 52-61 are directed towards methods for the production of HIV-2 hybridization probes corresponding to the regions disclosed supra.

The applicants broadly recited claim language does not adequately disclose the hybridization and washing conditions under which the purported probes would successfully detect HIV-2 RNA. The hybridization conditions and washing conditions are critical for hybridization studies. Said conditions will vary considerably depending upon the probe size, it's genomic location (i.e. LTR vs. *env*), G-C content, and the corresponding melting temperature (T_m). In

the absence of proper guidance said probes could display cross-hybridization to SIV, HIV-1, and cellular RNAs as well. Accordingly, one practicing the invention as currently claimed would incorrectly identify HIV-1 or SIV as HIV-2. This rejection may be obviated by clearly disclosing the hybridization and washing conditions (i.e. high stringency wash consisting of 0.1X SSC, 0.1% SDS at 65 degress for 30 min. or low stringency wash consisting of 2X SSC, 0.1% SDS at 50 degress for 30 min.) of the claimed method.

Additionally, the broadly recited claim language is directed towards any probe corresponding to HIV-2 RNA. However, the applicants only provide guidance pertaining to the nucleic acid sequences obtained from the HIV-2_{ROD} subclones dislosed in the specification. The applicants do not disclose any nucleic acids in addition to those specifically recited. This rejection may be obviated by limiting the claim language to HIV-2_{ROD} nucleic acid probes, by succinctly disclosing the source of the probe, the genomic location, and identifying the precise fragment utilized (i.e. an HIV-2_{ROD} LTR nucleic acid probe consisting of an *EcoRI*/*EcoRI* fragment of pSPE2).

Claims 45-49 and 55-59 recite HIV-2_{ROD} nucleic acid probes that comprise nucleotide sequences capable of encoding for a recited amino acid sequence. The degeneracy of the genetic code is well-recognized in the art. It has also been established that the lentivirinae display considerable genomic heterogeneity. The broadly recited claim language encompasses a myriad number of combinations. However, the applicants do not precisely identify any alternative nucleic acid sequences capable of encoding for the corresponding peptides. Accordingly, the claim language should be limited to those specific HIV-2 nucleic acid

sequences contained in the specification.

Claims 43 and 53 recite nucleic acid probes comprising cDNAs. The term "cDNA" is defined in the art as a product consisting of a double-stranded DNA sequence obtained by the *in vitro* enzymatic conversion (via reverse transcriptase) of mRNA into double-stranded DNA. However, the applicants only disclose the generation of one specific cDNA clone, pSPE2. The remaining nucleic acids (pROD 27-5, pROD 35-3, pROD 4.6, pROD 4.8, and pROD 4.7) described in the specification were generated from genomic DNA libraries and are not cDNA probes. Nucleic acid sequences corresponding to other cDNAs are not taught in the specification. Accordingly, the applicants should amend the claim language to recite the specific cDNA clone described in the specification.

When all of the aforementioned issues are considered in toto, it would require undue experimentation of one skilled in the art to ascertain all the scientific parameters required to practice the invention. Therefore, claims 42-61 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

20. Claims 42-61 are rejected under 35 U.S.C. § 112, second paragraph, as being vague and indefinite for failing to particularly point out and distinctly claim the invention. The phrase "nucleic acid corresponding to HIV-2 RNA" is vague and confusing. It is not readily manifest if the applicants are referring to an RNA, cDNA, or DNA probe derived from HIV-2, SIV, HIV-1, or some other source. Are the applicants referring to a certain degree of genetic identity (i.e. an $HIV\text{-}2_{ROD}$ cDNA probe

obtained from pSPE2 that contains 100% nucleic acid identity with the HIV-2 LTR)? Applicants should amend the claim language accordingly.

Claims 44-49 and 54-59 recite nucleic acids comprising a particular sequence or capable of encoding for a particular protein. However, these broad recitations are confusing since the applicants do not clearly identify the source of the nucleic acid and the corresponding probe. This rejection may be obviated by specifically reciting the source of the probe and its corresponding genomic location and coordinates (i.e. an HIV-2_{ROD} LTR cDNA probe obtained from pSPE2 depicted in Figure 6 consisting of nucleotides 1-380).

Claim 52 contains the phrase "recombinantly synthesizing a cloning vector" which is abstruse. It is not readily manifest if the applicants intend to actually synthesize the indicated cloning vector or if they are merely referring to the generation or construction of a recombinant plasmid containing the insert of interest. This rejection may be obviated by amending the claim language appropriately.

Claim 50 presented on page 22 of the preliminary amendment dated September 15, 1995, should be renumbered claim 60 for clarification.

21. The following is a quotation of the appropriate paragraph of 35 U.S.C. § 102 that forms the basis for the rejection under this section made in this action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

22. Claims 42 and 52, directed towards methods for detecting HIV-2 RNA and for producing HIV-2 hybridization probes, are rejected under 35

U.S.C. § 102(a) as being anticipated by Clavel et al. (1986, Science 233:343-346). Clavel et al. (1986) report the identification and isolation of a novel West African human retrovirus, designated LAV-II (or HIV-2). The authors conducted slot-blot hybridization studies on biological samples containing HIV-2 RNA (refer to Figure 5, page 346). The preparation of HIV-1 sub-genomic probes was disclosed. Said probes cross-hybridized, albeit weakly, with the HIV-2 RNA samples (refer to page 345, column three, lines 22-25 and page 346, column 1, lines 6-11). Since these nucleic acid probes hybridize to HIV-2 RNA, they clearly "correspond to HIV-2 RNA" and thereby meet the limitations of the instantly claimed invention.

23. Claims 42-44 and 52-54, directed towards methods for detecting HIV-2 RNA and for producing HIV-2 hybridization probes derived from the HIV-2 LTR, are rejected under 35 U.S.C. § 102(a) as being anticipated by Clavel et al. (1986, Nature 324:691-695). Clavel et al. (1986) describes the molecular cloning of the complete 9.5 kb genome of a novel retrovirus, the human immunodeficiency virus type 2 (HIV-2, previously designated LAV-2). The authors disclose the preparation of a cDNA HIV-2 probe, designated E2, and its use to detect the genomic RNA of HIV-2 (refer to page 691, column 2, lines 29-33 and page 693, Figures 2C and 2D). The nucleotide sequence of this probe (refer to Figure 1, page 692) is identical to nucleotides 78-380 of the sequence recited in claims 44 and 54 and thereby meets all the limitations of the open claim language.

24. The non-statutory double patenting rejection, whether of the

obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent (refer to *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993)).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d). Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

25. Claims 42-61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42-46 and 48-50 of copending application Serial No. 08/392,613. Although the conflicting claims are not identical, they are not patentably distinct from each other. The '613 application discloses isolated and purified HIV-2_{ROD} nucleic acids obtained from the *gag*, *env*, and LTR regions of the viral genome. The nucleotide sequences disclosed are identical to those presented in the instant application (refer to pages 56-61 and Figure 6). These nucleic acids clearly "correspond to HIV-2 RNA" and would be useful for the

detection of HIV-2 RNA in biological specimens. Accordingly, one of ordinary skill in the art would be motivated to utilize these nucleic acids in an *in vitro* diagnostic assay to identify HIV-2.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 42, 49-51, 52, and 59-61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 83 of copending application Serial No. 08/250,103. Although the conflicting claims are not identical, they are not patentably distinct from each other. The '103 application discloses an HIV-2_{ROD} cloned nucleic acid obtained from the *env* region of the viral genome. The nucleotide sequence disclosed is identical to the *env* sequence presented in the instant application (refer to pages 58-61 of the specification). This nucleic acid clearly "corresponds to HIV-2 RNA" and would be useful for the detection of HIV-2 in biological specimens. Accordingly, one of ordinary skill in the art would be motivated to utilize these nucleic acids in an *in vitro* diagnostic assay to identify HIV-2.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

27. Correspondence related to this application may be submitted to Group 1813 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax number for Group 1813 is (703) 305-7939.

28. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D. whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Friday from 8:30 AM to 5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ms. Christine Nucker can be reached at (703) 308-4028. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1813 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Group Art Unit 1813

November 30, 1995

ROBERT D. BUDENS
PRIMARY EXAMINER
GROUP 1800